Remarks

Status of the Claims

Claims 21-23 and 53-56 are pending. The Office Action identifies "claims 2, 4, and 13" as "non-elected species of Group I" and "claims 5-8 and 10-12" as "non-elected Groups II-IV." These statements appear to refer to a different application. Claims 1-20 of the present application were canceled in a preliminary amendment filed with the application.

Amendments to the Claims

Claim 1 is amended for clarity. The claim itself supports the amendments, which do not add new matter.

Substitute Sequence Listing

The Office Action requires a substitute sequence listing to include the sequences present in Figures 1B and 19. The substitute sequence listing that accompanies this paper differs from the sequence listing originally filed only in that it also contains the sequences present in Figures 1B and 19. I believe the contents of the computer readable form and the paper copy of the substitute sequence listing are identical.

The specification is amended to insert sequence identifiers in the descriptions of these figures. Neither the substitute sequence listing nor the amendments to the specification add new matter.

Listing of References in the Specification and Information Disclosure Statement

The Office Action notes that "[t]he listing of references in the specification is not a proper information disclosure statement." Office Action at page 3, item 6. Applicants did not intend this list to be a list of references material to patentability. Applicants identified references for the Examiner's consideration in an Information Disclosure Statement filed with the application. Applicants thank the Examiner for considering the references and returning the initialed Forms PTO-1449.

The Examiner was not able to consider one of the cited references (EP 0 352 761) because it is in German. An English language equivalent of EP 0 352 761 is cited in the Information Disclosure Statement that accompanies this paper.

The Objection to the Amendment Filed April 5, 2004

The preliminary amendment filed April 5, 2004 incorporated by reference into the present specification the disclosures of parent applications Serial No. 09/789,720 and 09/150,622. The Office Action contends that the incorporation by reference introduced "added material which is not supported by the original disclosure." Office Action at page 3, item 7.

The April 5, 2004 amendment did not add new matter. The present application is a division of Serial No. 09/789,720 which, in turn, is a division of Serial No. 09/150,622. Applicants incorporated the parent applications' disclosures into the present application in case any portion of the present specification was lost or inadvertently omitted when the application was filed. The disclosures of the three applications are identical. The incorporation by reference did not introduce any new matter into the present application's disclosure.

Priority Applications

The Office Action asserts that the claim recitations "bound to the surface of a cell" and "wherein the cell is a dendritic cell" are not supported in Applicants' earliest priority application Serial No. 60/058,573. Office Action at page 3, item 8. Claims 13 and 14 of Serial No. 60/058,573 are virtually identical to claims 21 and 22 of the present application:

Serial No. 60/058,573	present application
Claim 13. A composition comprising a cell in which a chimeric protein has been bound to the surface of the cell, wherein the chimeric protein comprises an MHC molecule and an immunoglobulin chain, wherein the chimeric protein associates to form molecular complexes comprising at least two chimeric proteins per complex, wherein an antigenic peptide is bound to each MHC molecule, wherein each MHC molecule within the molecular complex is bound to an identical antigenic peptide.	Claim 21 (as amended). A composition comprising a cell in which at least two chimeric proteins are bound to the surface of the cell, wherein each chimeric protein a polypeptide of an MHC molecule and an immunoglobulin chain; wherein the at least two chimeric proteins associate to form a molecular complex, wherein an identical antigenic peptide is bound to each MHC polypeptide within the molecular complex.
Claim 14. The composition of claim 13 wherein the cell is a dendritic cell.	Claim 22. The composition of claim 21 wherein the cell is a dendritic cell.

The present claims are therefore entitled to the September 11, 1997 priority date of Serial No. 60/058,573.

Rejections Under 35 U.S.C. § 102

Claims 21 and 23 stand rejected as anticipated by WO 96/04314 under 35 U.S.C. §§ 102(b), 102(e), and 102(a).[1] Claims 21-23 stand rejected as anticipated by U.S. Patent 5,869,270 under 35 U.S.C. § 102(e). Applicants respectfully traverse the rejections.

A reference cited under 35 U.S.C. § 102 must expressly or inherently describe each element set forth in the rejected claim. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Independent claim 21 is directed to a composition comprising a cell which has at least two chimeric proteins bound to its surface. The chimeric proteins each comprise a polypeptide of an MHC molecule and an immunoglobulin chain and they associate to form a molecular complex. An identical antigenic peptide is bound to each MHC polypeptide within the molecular complex.

Neither WO 96/04314 nor the '270 patent explicitly or inherently teaches the claimed composition. Both documents teach fusion proteins comprising a single chain of an MHC molecule and an antigen (page 5, lines 1-8 of WO 96/04314; col. 2, lines 26-31 of the '270 patent). The disclosed "MHC fusion complex" can be fused to the constant region of an immunoglobulin (*e.g.*, Figure 1C of each document); this configuration, however, is used only when the complex is to be secreted (*i.e.*, solubly expressed):

> For example, for expression of a truncated fusion complex, specifically a ***soluble*** MHC fusion complex that does not contain transmembrane or cytoplasmic portions and is linked to an immunoglobulin such as IgG, the PCR product preferably includes IgG splice sites and leader sequences necessary for proper expression ***and secretion*** of the MHC-immunoglobulin fusion complex.

[1] For the sake of accuracy, WO 96/04314 cannot be cited under 35 U.S.C. § 102(e). WO 96/04314 was filed July 31, 1995. Second § 102(e) applies to published PCT applications filed on or after November 29, 2000.

Page 12, line 30, to page 13, line 4 of WO 96/04314; col. 8, lines 42-48 of the '270 patent (emphasis added). See also page 19, lines 17-20 of WO 96/04314 and col. 12, lines 12-16 of the '270 patent (emphasis added): "***For soluble expression***, the α1-α2 and peptide-linked β1-β2 domains are suitably fused to an immunoglobulin, preferably to the constant domains of the immunoglobulin kappa and heavy chains, respectively, as depicted in FIG. 1C." Finally, see Example 2 of each document: "The following protocol includes expression of ***soluble*** peptide-linked MHC class II/immunoglobulin molecules as chimeric protein."

Neither WO 96/04314 nor the '270 patent discloses a composition comprising a cell with at least two chimeric proteins bound to its surface, wherein each chimeric protein comprises an MHC molecule and an immunoglobulin chain and associate to form a molecular complex. Thus, neither document anticipates the claimed composition.

Applicants respectfully request withdrawal of the rejection.

Rejections Under 35 U.S.C. § 103(a)

The Office Action makes five rejections under 35 U.S.C. § 103(a):

- claims 21-23 and 53 over WO 98/03552 in view of Celluzzi,[2] Liu,[3] and Bendig;[4]
- claims 21-23 and 53-56 over WO 98/03552 in view of Celluzzi, Liu, and Utz; [5]
- claims 21-23 and 53 over WO 96/04314 in view of Celluzzi, Liu, and Bendig;
- claims 21-23 and 53-56 over WO 96/04314 in view of Celluzzi, Liu, and Utz; and
- claims 21-23 and 53-56 over U.S. Patent 5,869,270 in view of Utz and Liu.

Applications respectfully traverse the rejections.

Rejections based on WO 98/03552

WO 98/03552 is not prior art to the present application. Section 102(e) of 35 U.S.C. applies to published PCT applications filed on or after November 29, 2000. WO 98/03552 was filed July 15, 1997. Thus, the effective date of WO 98/03552 as a reference is its publication date, January 29, 1998. As explained above, the claimed invention is entitled to an effective

[2] Celluzzi *et al.*, *J. Exp. Med. 183*, 283-87, 1996.

[3] Liu *et al.*, *J. Exp. Med. 185*, 165-70, January 6, 1997.

[4] Bendig, Methods: A Companion to Methods in Enzymology, vol. 8, pages 83-93, 1995.

[5] Utz *et al.*, *J. Virol. 70*, 843-51, 1996.

filing date of September 11, 1997 based on its disclosure in Serial No. 60/058,573. This moots both rejections based on WO 98/03552.

Rejections based on WO 96/04314 or the '270 patent

The U.S. Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of obviousness. The *prima facie* case requires three showings:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Manual of Patent Examining Procedure, 8th ed., § 2142. In this case, the ordinary artisan would not have been motivated to modify the primary references as the Office Action contends.

The disclosures of WO 96/04314 and the '270 patent are discussed above in connection with the rejections under 35 U.S.C. § 102. Celluzzi is cited as teaching the basic biology of antigen presenting cells and their function in presenting antigen to prime cytotoxic T lymphocyte (CTL) responses. Liu is cited as teaching an IgG1 isotype monoclonal antibody. Bendig is cited as teaching humanization of rodent antibodies. Utz is cited as teaching that most HLA-A2 positive individuals with HTLV-1 associated HAM-TSP have CTLs which recognize the HTLV-1 tax 11-19 peptide. Even if, *arguendo*, properly combined, none of the cited combinations teach or suggest the claimed composition.

First, the recited chimeric proteins in the claimed compositions "associate to form a molecular complex." Claim 21. In contrast, both of the primary references clearly teach that single chain fusions are preferred over complexes. See page 21, lines 14-18 of WO 96/04314 (emphasis added):

> As discussed above, single chain MHC fusion complexes of the invention are also preferred, i.e. a fusion complex that ***consists of a single polypeptide rather than a multiple chain aggregate*** such [ ] the native heterotrimeric class II/peptide complex where α and β chains and a peptide are associated through non-covalent interactions.

See col. 13, lines 13-16 of the '270 patent (emphasis added):

> As discussed above and in said PCT Application [WO 96/04314], single chain MHC fusion complexes are desirable, i.e. a fusion complex that ***consists of a single polypeptide rather than a multiple chain aggregate*** such [ ] the native heterotrimeric class II/peptide complex where α and β chains and a peptide are associated through non-covalent interactions.

Second, the chimeric proteins recited in the pending claims (a) comprise an MHC molecule and an immunoglobulin chain and (b) are bound to a surface of a cell. Both WO 96/04314 and the '270 patent teach binding to a cell surface only for single chain MHC-antigen fusions. For example, both documents only teach use of cells in connection with MHC fusions which do not contain immunoglobulin chains. *See, e.g.*, Examples 13 and 14 of each document. Both WO 96/04314 and the '270 patent teach inclusion of an immunoglobulin chain only when an MHC fusion complex is solubly expressed (*i.e.*, secreted).[6]

The teachings of the cited references must be considered as a whole and compared with the subject matter of the rejected claims. *Graham v. John Deere* 383 U.S. 1, 17 (1966). As a whole, each primary reference clearly teaches that single chain fusion proteins are preferred. Each primary reference only teaches binding of single chain fusion proteins on a cell surface. Each primary reference teaches inclusion of an immunoglobulin chain in an MHC fusion only for soluble expression (*i.e.*, secretion). The ordinary artisan would not have ignored these

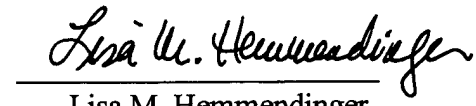
[6] See col. 8, lines 42-48 and col. 12, lines 12-16 of the '270 patent of the '270 patent; page 12, line 30, to page 13, line 4 and page 19, lines 17-20 of WO 96/04314; and Example 2 of both documents. These sections are quoted above.

explicit teachings. No possible combination of any of the cited secondary references directs one of ordinary skill to modify the teachings of either WO 96/04314 or the '270 patent. The ordinary artisan therefore would not have been motivated to modify the cited primary references as the Office Action suggests.

The Office Action does not make a *prima facie* case that any of claims 21-23 and 53-56 are obvious. Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

Date: March 29, 2006

By: 

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